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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/694,534 | 10/27/2003 | Alex Aronov | VPI/02-114 US | 1905 |

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VERTEX PHARMACEUTICALS INC.
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EXAMINER

AULAKH, CHARANJIT

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1625

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--|--------------------------------------|--|
| Office Action Summary | Application No. 10/694,534 | Applicant(s) ARONOV ET AL. | |
| | Examiner Charanjit S. Aulakh | Art Unit 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-49,51-63 and 85-90 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-33,36-49,51-58,60-63 and 85-90 is/are rejected.
- 7) ☒ Claim(s) 34,35 and 59 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. According to paper filed on July 26, 2005, the applicants have elected group I without traverse for further prosecution in response to restriction requirement. The applicants have also canceled claims 2, 3 and 64-84 and furthermore, have amended claims 1, 36, 38, 61 and 63.
2. Claims 1, 4-49, 51-63 and 85-90 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 86 and 88-90 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands*, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation

necessary, the amount of direction or guidance provided, the state of the prior art, the presence of working examples and the breadth of claims.

The specification teaches inhibition of GSK-3, Aurora-2, CDK-2, ERK-2, PRAK, SRC, SYK and MK2 in vitro by instant compounds (see pages 216-221). Based on these teachings, the instant compounds will have utility in treating only those specific disease conditions where inhibitors of GSK-3, Aurora-2, CDK-2, ERK-2, PRAK, SRC, SYK and MK2 activity are well known in the prior art (before the effective filing date of instant application) to have therapeutic utility. However, there is no teaching either in the specification or prior art references provided showing well known utility of inhibitors of GSK-3, Aurora-2, CDK-2, ERK-2, PRAK, SRC, SYK and MK2 activity alone or in combination with any other therapeutic agent. There are no working examples present showing efficacy of instant compounds alone or in combination with any other therapeutic agent in known animal models of any disease condition. The instant compounds of formula I encompasses millions of compounds based on the values of variables R1-R5, Q1, Q2, A, Y and every known therapeutic agent in the art and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the effectiveness of instant compounds alone as well as in combination with every known therapeutic agent in known animal models of all known cardiovascular diseases, diabetes, neurological disorders, immunodeficiency disorders, allergic diseases, inflammatory diseases, autoimmune diseases, viral diseases etc. and hence their utility for treating these disorders.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 4-33, 36-49, 51-58, 60-63 and 85-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 4-33, 36-49, 51-58, 60-63 and 85-90, the value of variable RA is not defined. Actually, recent amendment deleted the definition of this variable.

In claim 7, the value of ring A is defined as formulae II-A through II-DD. However, there is no formula II-DD. Actually, formula II-BB is mentioned twice on page 8.

Claim 8 recites the limitation "II-DD for ring A" in claim 7. There is insufficient antecedent basis for this limitation in the claim.

Regarding claims 15, 16 and 89, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In claims 20, 21, 45 and 46, the value of variable R defined as ---generally above and in classes and subclasses herein----- is vague and indefinite since actual intent is not clear.

Claim 26 recites the limitation " formula h' " in claim 20. There is insufficient antecedent basis for this limitation in the claim.

Claim 30 recites the limitation " hydrogen, methyl, ethyl, cyclopropyl, hydroxyl, phenyl or CH₂NH₂ for the value of variable R₃ " in claim 27. There is insufficient antecedent basis for this limitation in the claim.

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Claim 38 recites the limitation " formulae i-x and II-A to II-DD for ring A " in one of the claims 33-37. There is insufficient antecedent basis for this limitation in the claim.

Claim 38 recites the limitation " CHR6 for the value of variable Z " in one of the claims 33-37. There is insufficient antecedent basis for this limitation in the claim.

Claim 63 recites the limitation " CHR6 for the value of variable Z " in one of the claims 58-62. There is insufficient antecedent basis for this limitation in the claim.

In claim 86, the term ----therapeutic agent ---- is indefinite since specific agents are not defined.

In claim 87, the term ---family--- is vague and indefinite since actual intent is not clear.

What are the other family members?

In claim 88, the term ----mediated disease or condition--- is indefinite since specific diseases are not defined.

In claim 89, the terms---cardiovasculae diseases, neurological disorders, immunodeficiency disorders, inflammatory diseases, allergic diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, infectious diseases and viral diseases----- are indefinite since specific diseases are not defined.

In claim 90, the terms ---anti-proliferative agent, anti-inflammatory agent, an immunomodulatory agent, a neurotrophic factor, an anti-infective agent, an anti-viral agent and an agent for treating cardiovascular disease ----- are indefinite since specific agents are not defined.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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7. Claims 1, 39, 52-56, 85, 88 and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel (Biorgan. & Medicin. Chem. Lett.).

Patel discloses Unsymmetrical cyclic ureas as HIV protease inhibitors for treating HIV infection. The tautomer compounds 3 and 6 (see page 3218) disclosed by Patel anticipates the instant claims when Q1 represents $-C(RA)_2$ and Q2 represents $-C(RC)_2$ in the instant compounds of formula I.

Allowable Subject Matter

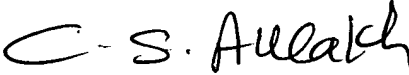
8. Claims 34, 35 and 59 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Charanjit S. Aulakh
Primary Examiner
Art Unit 1625